External validation of the Endovascular aneurysm repair Risk Assessment model in predicting survival, reinterventions, and endoleaks after endovascular aneurysm repair

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Objective: **The Endovascular aneurysm repair Risk Assessment (ERA) model predicts survival (early death, 3-year survival, and 5-year survival), reinterventions, and endoleaks after elective endovascular aneurysm repair. We externally validated the ERA model in our cohort of patients.**

Methods: **This was a retrospective validation study of 433 consecutive patients with an asymptomatic abdominal aortic aneurysm treated with endovascular aneurysm repair in three hospitals (Amsterdam, The Netherlands) between 1997 and 2010. The area under the receiver operating characteristic curve was used as measure of accuracy (>0.70 was considered as sufficiently accurate).**

Results: **The early death rate was 1% (3 of 433; 95% confidence interval [CI], 0%-2%), the 5-year survival rate was 65% (95% CI, 61%-70%), the 5-year reintervention rate was 18% (95% CI, 14-78%), and the 5-year rate of type I, II, or III endoleak was 25% (95% CI, 20%-29%). The areas under the curve varied between 0.64 and 0.66 for predictions of survival and between 0.47 and 0.61 for reinterventions and endoleaks.**

Conclusions: **The predictions of survival, reinterventions, and endoleaks made by the ERA model were not sufficiently accurate to be used in our clinical practice. (J Vasc Surg 2014;59:1555-61.)**

During the past two decades, the treatment of abdominal aortic aneurysms (AAAs) has been subject to change. Conventional open repair (OR) has been partially substituted by endovascular aneurysm repair (EVAR). Recent clinical trials have shown that 30-day mortality is lower after EVAR than after OR.[1-3] However, the incidence of reinterventions and endograft-related complications is higher after EVAR than after OR. A challenge in current clinical practice is to determine which of the treatments will benefit the patient most: OR, EVAR, or nonoperative therapy. Prediction models are helpful in assessing individual outcomes after intervention and can support clinical decision making for elective aortic surgery.

A promising prediction model is the EVAR Risk Assessment (ERA) model. The ERA model includes only eight preoperative variables (Table I).[4,5] The ERA model has been designed to predict survival-related outcomes (30-day death, 3-year and 5-year survival, and aneurysm-related death), the need for reintervention, type I and type II endoleaks, and other complications, including technical success, graft complications, migration, and conversion. In aortic surgery, many models have been developed predicting the 30-day or in-hospital death rate and reinterventions or complications separately. Until now, the ERA model is the only one that predicts all of these outcomes together. These combined predictions are a major advantage that could potentially support decision making. The model was validated on three occasions: internally, using bootstrapping in the original Australian cohort and externally in the United Kingdom[6] and in Australia.[7] The predictions of survival (30-day, 3-year, and 5-year) and type I endoleak (30-day and midterm) were sufficiently accurate. The ERA model is freely available at http://health.adelaide.edu.au/surgery/evar/predictive.html or for a small fee as an iPhone application.

The primary objective of the present study was a third external validation of the ERA model using a Dutch cohort of patients. A secondary objective was the identification of preoperative variables that might improve the ERA model.

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Table I. Baseline characteristics and the preoperative variables included in the EVAR Risk Assessment (*ERA*) model

Baseline characteristics	*Value*	*Variable included in the ERA model?*
Sex		Yes
Male	89 (386)	
Female	11 (47)	
Age, years	73.9 ± 7.4	Yes
BMI, kg/m^2	26.1 ± 3.8	No
Current smoking	43 (155/359)	No
Comorbidity		
Cardiac (SVS/ISCS score ≥1)	59 (246/420)	No
Cerebrovascular (SVS/ISCS score ≥1)	13 (57/429)	No
Previous history of malignancy	23 (101/433)	No
ASA score ≥3	60 (261/433)	Yes
GAS	80 ± 10	No
Anemia	26 (111/424)	No
Serum creatinine, μmol/L	88 (75-105)	Yes
Max aneurysm diameter, mm	62 ± 11	Yes
Infrarenal neck, mm		
Length	33 ± 13	Yes
Diameter	24 ± 3	Yes
Aneurysm angulation ≥45°	19 (67/349)	Yes
Late generation endograft	55 (220/399)	No
Adjunctive procedure	20 (86/433)	No

ASA, American Society of Anesthesiologists; *BMI,* body mass index; *EVAR,* endovascular aneurysm repair; *GAS,* Glasgow Aneurysm Score; *ISCS,* International Society for Cardiovascular Surgery; *IQR,* interquartile range; *SD,* standard deviation; *SVS,* Society for Vascular Surgery.
Continuous data are presented as mean ± standard deviation or median (IQR) and categorical data as percentage (number).

METHODS

We conducted a retrospective cohort study at the Academic Medical Centre (tertiary university hospital), at the Onze Lieve Vrouwe Gasthuis (teaching hospital), and at the VU University Medical Centre (tertiary university hospital) in Amsterdam, The Netherlands. Included were all consecutive patients with EVAR for an asymptomatic aneurysm of the infrarenal abdominal aorta between January 1, 1997, and January 1, 2010. Patients with an inflammatory aneurysm were excluded.

All patients had routine follow-up, according to local practice, with yearly computed tomography angiography (CTA) or duplex ultrasound imaging combined with plain abdominal X-ray imaging. Patient follow-up was assessed up to July 1, 2012. Primary end points were death, reinterventions, and type I, II, and III endoleaks. The outcomes of 30-day death, 3-year survival, and 5-year survival will be referred to as the "survival-related outcomes." The present study focused on the validation of the predictions of these survival-related outcomes, reinterventions, and endoleaks by the ERA model. Because of a very low number of autopsies, cause of death was considered to be unreliable, and we did not validate the predictions of aneurysm-related death. Because of the retrospective design, we did not validate the predictions of technical success, graft complications, migration, and conversion.

Data collection. Data were collected from medical records, discharge documents, preoperative anesthesia assessment records, and operative reports. Data were entered by the first author using Office Access 2003 (Microsoft Corp, Redmond, Wash) and included field limits and multivariate checks. Patients were identified from a prospective registry (Academic Medical Centre) and from the financial coding administration of interventions (Onze Lieve Vrouwe Gasthuis and VU University Medical Centre).

Definitions of preoperative variables[8] and postoperative outcomes[9] were in accordance with the reporting standards of the Society for Vascular Surgery and the International Society for Cardiovascular Surgery (SVS/ISCS) and the article first describing the ERA model.[4] Early death was defined as the 30-day death rate. Reinterventions and endoleaks were assessed twice postoperatively: as defined by the ERA model, "initial" encompassed the first 30 days, and "midterm" referred to the period between 30 days and 5 years.

As in the ERA model, conversions to OR were separately analyzed from reinterventions, and type III endoleaks were included as type I in the statistical analysis. Anemia was defined as hemoglobin <134 g/L (<8.4 mmol/L) in men and <117 g/L (<7.3 mmol/L) in women. A previous history of malignancy included all types of cancer except nonmelanoma dermal carcinoma.

Endografts were dichotomized into early generation and late generation. Early generation encompassed the endografts formerly used in daily practice, which were the Lifepath (Edwards Lifesciences, Irvine, Calif) in 6, the Ancure (Endovascular Technologies, Menlo Park, Calif) in 8, the Talent (Medtronic, Minneapolis, Minn) in 100, the AneuRx (Medtronic) in 45, and an investigational Cordis endograft (Johnson & Johnson, New Brunswick, NJ) in 4. The late generation encompassed endografts currently used in daily practice, which are the Zenith (Cook Medical, Bloomington, Ind) in 196, the Endurant (Medtronic) in 24, and the Gore Excluder (W. L. Gore & Associates, Flagstaff, Ariz) in 16.

Aneurysm characteristics were measured in the sagittal, coronal, and axial planes of the preoperative CTA. Date of death was obtained from medical records and general practitioner registers.

Statistical analysis. The statistical analysis was done using SPSS 19.0 software (IBM Inc, Armonk, NY) and R (The R Foundation for Statistical Computing, Boston, Mass). Continuous data are described by the mean with corresponding standard deviation for data normally distributed, and by the median with corresponding interquartile range (IQR) for data with a skewed distribution. The 5-year survival, reintervention, and endoleak rates were estimated by Kaplan-Meier survival analyses and compared with use of the log-rank test. Also reported are the actual outcome rates in patients treated before July 1, 2007.

The statistical analysis comprised three steps. First, the accuracy of the ERA model was assessed for discrimination and calibration. Discrimination is the ability of a model to distinguish between an event and no event; for example, between dying and surviving patients. Discrimination was assessed using the area under the receiver operating characteristic curve (AUC), specifically using the Harrell *C* statistic,[10] which takes into account patients who are censored before the end point. An AUC of >0.70 is generally considered sufficiently accurate. Calibration refers to the agreement between predicted and observed outcomes and was assessed by plotting the predicted outcomes in quintiles with the corresponding observed outcomes. Calibration was assessed for 3-year and 5-year survival and included only patients who had the intervention before July 2009 and July 2007 to ensure sufficient follow-up time.

Second, preoperative variables that might improve the predictions of survival-related outcomes of the ERA model were identified using a Cox proportional hazards model. First, a univariable survival analysis was done including variables identified after a thorough literature search. The variables were:

- Patient-related: age,[11] sex,[12] renal impairment,[11] pulmonary impairment,[13] cardiac impairment,[14] diabetes, hypertension, malignancy,[14] smoking, body mass index (BMI), anemia,[15] and the American Society of Anesthesiologists (ASA) Physical Status Classification score[11];
- Aneurysm-related: maximum aneurysm diameter,[11,16] aortic neck diameter, length, and angulation,[11] and iliac artery calcification; and
- Operation-related: anesthesia,[17] adjuvant surgical procedures,[18] and endograft generation.[12]

Subsequently, the variables with a *P* value of <.20 in the univariable analysis and <15% missing data were included in the Cox proportional hazards model (stepwise backward method). The variables of the ERA model were forced into the Cox proportional hazards model to identify variables with additional value. The −2 log likelihood (−2LL) was reported to represent Cox model performance. A lower −2LL represents better fit of a multivariable model. The difference between Cox models was tested with use of the −2LL in a χ^2 distribution.

Third, a sensitivity analysis was done to explore the influence of the use of different endograft generations (early vs late) on the outcomes. The sensitivity analysis included AUC assessment per endograft generation and two multivariable Cox proportional hazard models to assess the association between endograft generation and reinterventions. The first Cox model used the end point reintervention, including conversion, and the variables infrarenal neck angulation, diameter, and length were included to adjust for aortic anatomy-related confounding. In the second Cox model, the outcomes reintervention and dying were combined to a composite end point to prevent bias from a competing risk of dying before a reintervention. The variables age, sex, previous history of malignancy, ASA 3 or 4, year of intervention, AAA diameter, and infernal neck angulation, diameter, and length were included to adjust for survival- and anatomy-related confounding.

Missing values. Of the 434 patients studied, ASA scores were missing in 40 (9%) and were imputed with ASA score 3, and serum creatinine levels were missing in three (1%) and were imputed with the mean serum creatinine of the cohort. The preoperative CTA was available in 80% (349 of 434) of the patients. In the patients without a CTA, the aneurysm diameter was collected from the medical records. In these patients, the infrarenal neck length, diameter, and angulation were missing, and the predictions of reinterventions and endoleaks were excluded from the analysis. Therefore, the predictions of the survival-related outcomes were validated in 433 patients and of the reinterventions and endoleaks in 349 patients. An imputation procedure for the missing data was considered but not done because of the amount of missing data.

Ethics Committee approval. This study was conducted in accordance with the principles of the Declaration of Helsinki. The Medical Ethics Committee determined approval was not required because of the observational design.

RESULTS

A total of 433 patients with an asymptomatic AAA were treated with EVAR. The median follow-up time was 4.8 years (IQR, 2.9-5.0 years), 86 of 433 patients (20%) did not reach 5-year follow-up, and eight (2%) were lost to follow-up. Baseline characteristics are reported in Table I. The early death rate was 1% (3 of 433; 95% confidence interval [CI], 0%-2%), the 5-year survival rate was 65% (95% CI, 61%-70%), the 5-year reintervention rate was 18% (95% CI, 14%-22%), and the 5-year rate of type I, II, or III endoleak was 25% (95% CI, 20%-29%; Table II). The actual outcome rates in patients treated before 2007 were comparable to the estimations by the Kaplan-Meier survival analysis.

External validation. The AUC (representing the discrimination of the predictions by the ERA model) was 0.64 (95% CI, 0.19-1.0) for early death, 0.66 (95% CI, 0.60-0.72) for 3-year survival, and 0.66 (95% CI, 0.61-0.71) for 5-year survival (AUCs are shown in Fig 1). The AUC of the predictions for initial reintervention was 0.55 (95% CI, 0.42-0.68) and for midterm reintervention was 0.60 (95% CI, 0.51-0.69). The AUC of the predictions for initial type I endoleak was 0.61 (95% CI, 0.37-0.85) and for midterm type I endoleak was 0.59 (95% CI, 0.43-0.75). The AUC of the predictions for initial type II endoleak was 0.50 (95% CI, 0.41-0.59) and for midterm type II endoleak was 0.47 (95% CI, 0.36-0.58). The calibration plot of 3-year survival showed that the agreement between predicted and observed survival was accurate (Fig 2). The calibration plot of 5-year survival showed an overestimation of survival by the predictions. A predicted 5-year survival of 50%, of 66%, and of 80% corresponded with an observed 5-year survival of 39% (95% CI, 28-51%), 57% (95% CI, 45%-69%), and 68% (95% CI, 55%-78%), respectively.

Table II. Outcomes after endovascular aneurysm repair (EVAR)

General cohort outcomes	*Median (IQR) or % (No.)*
Follow-up time, years	4.8 (2.9-5.0)
Censored before 5-year follow-up	20 (86/433)
Lost to follow-up	2 (8/433)
ERA model outcomes	*% (No.) 95% CI*
Early death	1 (3) 0-2
3-year survival KM[a]	80 (87) 76-83
3-year survival actual[b]	80 (81/401) 76-83
5-year survival KM[a]	65 (137) 61-70
5-year survival actual[c]	65 (107/309) 60-70
Initial reintervention	4 (19) 3-7
Midterm reintervention	13 (57) 10-17
5-year reintervention KM[a]	18 (69) 14-22
5-year reintervention actual[c]	21 (64/310) 17-25
Initial endoleak type I	2 (9) 1-4
Midterm endoleak type I	4 (17) 2-6
Initial endoleak type II	11 (48) 8-14
Midterm endoleak type II	7 (31) 5-10
5-year endoleak type I, II, or III KM[a]	25 (108) 20-29
5-year endoleak type I, II, or III actual[c]	23 (71/311) 19-28
5-year conversion to OR[c]	9 (28/314) 6-13

CI, Confidence interval; *ERA,* EVAR Risk Assessment; *IQR,* interquartile range; *KM,* Kaplan-Meier; *OR,* open repair.
[a]Estimated by Kaplan-Meier survival analysis.
[b]Actual rate in patients treated before July 1, 2009.
[c]Actual rate in patients treated before July 1, 2007.

Cox proportional hazards model. Univariable analysis identified sex, age, BMI, cardiac and cerebrovascular comorbidity, previous history of malignancy, smoking, ASA score, serum creatinine, anemia, aneurysm diameter, length of the infrarenal neck, adjunctive or ancillary procedure during the operation, and endograft generation as possible predictors of death ($P < .20$; Supplementary Tables I and II, online only). Smoking, BMI, and length of the infrarenal neck were not included in the Cox proportional hazards model because of >15% missing data. Age and serum creatinine were dichotomized because of nonlinearity. Age, sex, cardiac comorbidity, previous history of malignancy, ASA score, serum creatinine, and aneurysm diameter were identified as independent predictors of survival ($P \leq .05$; Table III). The −2LL of the Cox model that included only the ERA variables was 1491. The −2LL of the Cox model that included the ERA variables, cardiac comorbidity, and previous history of malignancy was 1476 (−2LL difference 12, χ^2 with two with degrees of freedom, $P < .01$).

Sensitivity analysis. From 2003 onward, more patients were treated with a late-generation endograft than with an early-generation endograft. The median follow-up time was 4.2 years (IQR, 1.5-5.0 years) for patients with an early-generation endograft and 3.8 years (2.0-5.0 years) for those with a late-generation endograft ($P = .69$). After stratification for endograft generation, the AUCs changed minimally, but the CIs increased (data not shown). The 5-year reintervention rate, including conversions, was 29% (95% CI, 21%-37%) in patients with an early-generation endograft and 16% (95% CI, 10%-21%) in patients with a late-generation endograft ($P < .01$). After adjustment for aortic anatomy-related confounders, the risk of reintervention or conversion was lower in patients treated with a late-generation endograft (adjusted hazard ratio, 0.49; 95% CI, 0.29-0.84; Supplementary Table III, online only). After adjustment for survival-related and aortic anatomy-related confounders, the risk of reintervention or dying was lower in patients with a late-generation endograft than in patients with an early-generation endograft (adjusted hazard ratio, 0.58; 95% CI, 0.39-0.86; Supplementary Table IV, online only).

DISCUSSION

The present validation study shows that the predictions by the ERA model of survival, reinterventions, and endoleaks after EVAR were not accurate in our cohort of Dutch patients. The study was conducted as a first step toward prospective validation to determine long-term outcomes after treatment allocation with support of the ERA model. In such a prospective validation study, the question can be answered whether our arbitrary AUC cutoff value of 0.70 is sufficiently accurate to support decision making. However, because of our disappointing results, further studies assessing the effect of the present ERA model appear to be futile.

Prediction of survival. Our results for survival-related outcomes conflict with the conclusions of the previous validation studies.[4,6,7] An explanation might be the inclusion of relatively healthier patients in our cohort. The proportion of patients with an ASA score 3 or 4 was 60%, compared with 65% to 80% in previous validation studies. The mean preoperative serum creatinine level was 93 μmol/L compared with 106 to 118 μmol/L, respectively. Other preoperative variables, such as age, sex, and aortic anatomy did not differ substantially. Since the United Kingdom EndoVascular Aneurysm Repair 2 trial,[1] we have become less willing to intervene in high-risk patients. However, without data on rejection rates, this explanation is based on reasoning only; moreover, a reliable prediction model should take potentially healthier patients into account.

Another possible explanation for the disappointing accuracy of the ERA model is that the discriminative character of the currently included variables is limited. For this reason, we tried to identify possible additional predictive variables. The Cox proportional hazards model identified "cardiac comorbidity" (SVS/ISCS score ≥1) and "previous history of malignancy" as independent predictors of survival in our cohort. Beside commonly known predictors of survival, "previous history of malignancy" might be important to consider for long-term survival after EVAR. However, these results have to be interpreted with caution because of limitations that we will discuss later. Future studies should determine the definite role of the variable "previous history of malignancy."

For the outcome early death, two new predictions models have been developed recently[19,20] and have shown

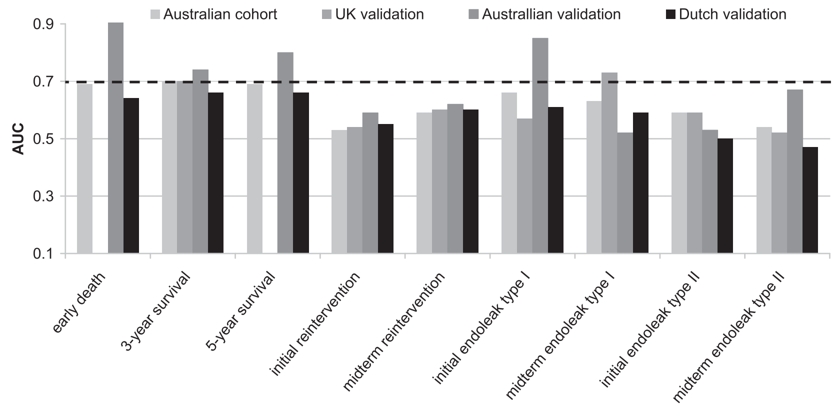

Fig 1. The area under the curve (*AUC*) (representing discrimination) of the predictions of survival, reinterventions, and endoleaks by the EVAR Risk Assessment (ERA) model in the original Australian audit cohort and in the validations in the United Kingdom (*UK*), Australia, and The Netherlands. An AUC >0.70 was considered as sufficiently accurate (indicated by the *bold dashed line*). *EVAR,* Endovascular aneurysm repair.

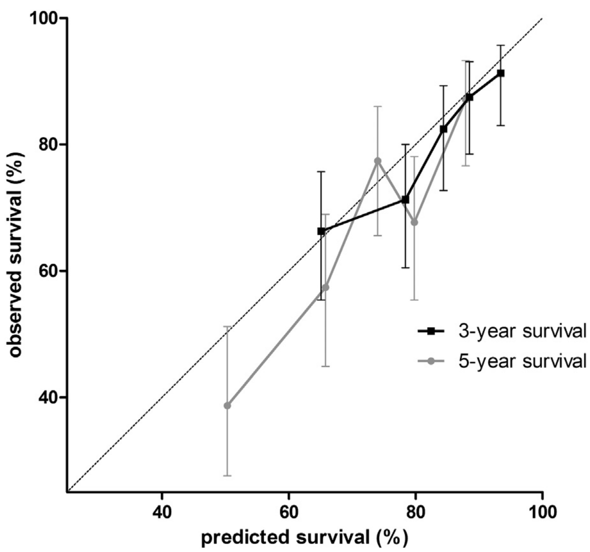

Fig 2. Calibration plots of the predicted 3-year and 5-year survival and the corresponding observed survival. Only patients with an intervention before July 2009 (3-year survival) or July 2007 (5-year survival) were included to ensure sufficient follow-up time. The *range bars* indicate the 95% confidence interval (CI) and the *diagonal dashed line* corresponds with ideal calibration.

sufficiently accurate predictions in external validation studies.[21,22] Possibly, these two models have more additional value in our clinical practice than the ERA model.

For 3-year and 5-year survival, the ERA model is the most accurate model currently available. The combined interpretation of the AUCs of all validations done so far might be interpreted as sufficiently accurate for 3-year survival (AUCs ranging in all validations between 0.66 and 0.74) and 5-year survival (AUCs in all validations ranging between 0.66 and 0.80).

Table III. Multivariable Cox proportional hazards model (stepwise backward method) for survival after endovascular aneurysm repair (EVAR)[a]

Variable	*Hazard ratio*	*95% CI*	P
Age ≥79 years	1.60	1.11-2.30	.01
Male sex	0.55	0.33-0.92	.02
Cardiac comorbidity (SVS/ISCS score ≥1)	1.47	1.01-2.15	.05
Previous history of malignancy	2.02	1.39-2.93	<.01
ASA 3 or 4	2.00	1.32-3.03	<.01
Creatinine >104 μmol/L	1.44	1.00-2.07	.05
Aneurysm diameter (per 5 mm)	1.12	1.04-1.21	<.01

ASA, American Society of Anesthesiologists; *CI,* confidence interval; *ISCS,* International Society for Cardiovascular Surgery; *IQR,* interquartile range; *SD,* standard deviation; *SVS,* Society for Vascular Surgery.
[a]The model included 420 patients and 133 events, −2 log likelihood (LL), 1476.

Prediction of reinterventions and endoleaks. Our results on prediction of reinterventions and endoleaks correspond with the conclusions in the previous validation studies.[4,6,7] Combined interpretation of the AUCs of for the reinterventions and endoleaks cannot be interpreted as sufficiently accurate. A probable explanation is that the ERA model is based on an audit conducted between 1999 and 2001, which is quite some time ago. Clinical practice has changed since the audit, especially in diagnosis and treatment of endoleaks. Moreover, the indication for a reintervention varies between hospitals. Without standardized treatment protocols, any model aiming to predict reinterventions has to overcome this variation.

Clinical practice has changed since the Australian audit also with regard to types of endografts. This might be another reason the predictions of reinterventions and endoleaks were not accurate. Our cohort includes a large number of patients with early-generation endografts. The ERA model aims to predict outcomes after all types of endografts. Our cohort includes seven different types of endografts, which is consistent with that aim. The sensitivity analysis showed that the accuracy of the predictions by the ERA model barely differed stratified for endograft generation. In accordance with recent results,[23] the reintervention rate was higher in early-generation endografts than in late-generation endografts. After adjustment for possible confounders, the risk of dying or reintervention was lower in patients treated with a late-generation endograft. These results indicate that new-generation endografts have improved outcomes.

The ERA model focuses on aortic neck characteristics for the prediction of reinterventions and endoleaks. Next to the Australian audit, the importance of the aortic neck for reinterventions and endoleaks has been reported from the European Collaborators on Stent-Graft Techniques for Abdominal Aortic Aneurysm Repair (EUROSTAR) registry[24,25] and confirmed in more recent studies.[26,27] This shows that anatomic characteristics associated with these predictions of the ERA might still be valid. However, two other models aiming to predict reinterventions also include other anatomic characteristics of the aortic neck (calcification), of the aneurysm (angulation, branch vessels, diameter, tortuosity), and of the iliac arteries (angulation, calcification, diameter, length, and tortuosity).[28,29] Possibly, these two models have more additional value in our clinical practice than the ERA model.

The identification of anatomic predictors of reinterventions and endoleaks was not possible in our cohort because of too few adverse events. This problem might be addressed by combining the data sets of all validation studies to the ERA model done so far for a "meta-regression." The number of adverse events would be increased, and a multivariable analysis might identify other independent predictors of outcomes. To increase reproducibility of the measurements of aortic anatomy, an automatically generated central lumen line might be relevant.[30] Current methods of measurement, using sagittal and coronal reconstruction in the CTA, might be too observer-dependent.

Limitations. Despite the high number of patients included in our validation of the ERA model, a limitation was the low event rate for the outcomes of early death and initial type I endoleak. For this reason, the CIs are wide surrounding the AUCs, and the point estimates should be interpreted with caution. All previous validation studies have this limitation, which might be addressed by combining the data sets for a "meta-validation."

The retrospective design resulted in missing data. The amount of missing data for the validation of the ERA model was 1% of serum creatinine, 9% of ASA scores, and 20% of CTAs. The reason for the large proportion of missing CTAs was that in one hospital, only images on sheets were available before 2006. Comparing patients with and without a preoperative CTA showed that the 5-year survival rate was 66% (95% CI, 60%-71%) vs 65% (95% CI, 55%-75%; $P = .97$), the 5-year reintervention rate was 19% (95% CI, 14%-23%) vs 18% (95% CI, 9%-26%; $P = .90$), and the 5-year endoleak rate was 26% (95% CI, 21%-31%) vs 19% (95% CI, 10%-27%; $P = .21$), respectively. Because these outcomes are comparable, we expect little effect of the missing CTAs on the conclusions.

The Cox proportional hazards models also suffered from missing data. Possible confounding factors, such as smoking, BMI, and the length of the infrarenal aortic neck, had to be excluded from the Cox model identifying additional predictors of survival after EVAR (Table III). Another limitation of this model was that our literature search for inclusion of variables might have failed to identify all predictors. For example, the use of medication or a preoperative electrocardiogram[15] might be of importance. A large group of patients (27%) had to be excluded from the Cox models in the sensitivity analysis (Supplementary Tables III and IV, online only). For these reasons, we are reluctant to draw definite conclusions from the results of the Cox models.

In patients in whom decision making is difficult, risk-assessment by a prediction model has the most additional value. For example, EVAR can be more challenging in patients with hostile aortic anatomy, and the risk of reinterventions and endoleaks is higher. OR is a reasonable alternative in these patients, and risk-assessment with a prediction model might support making the decision. Our validation study was too small to assess the accuracy of the ERA model in a subgroup of patients with hostile anatomy; however, this should be an important consideration in future studies developing or validating prediction models.

The primary objective of a vascular surgeon with EVAR is the prevention of rupture and aneurysm-related death. A final limitation of our study was that we could not objectify this aim by the validation of the predictions of aneurysm-related death. The ERA model predictions of 3-year and 5-year survival only correspond to the population-related survival after EVAR. From a patient's perspective, however, the cause of death is not important and the population-related survival suffices.

CONCLUSIONS

This study is the third and largest external validation of the ERA model. The predictions of early death, 3-year survival, 5-year survival, reinterventions, and type I, II, and III endoleaks were not sufficiently accurate to be used in our clinical practice. A multicenter prospective study is underway in Australia that aims to improve the predictive accuracy of the ERA model. We hope the results of this study will produce a model that can support decision making in our clinical practice.

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AUTHOR CONTRIBUTIONS

Conception and design: SvB, DL, RB
Analysis and interpretation: SvB, DL, AV, WW, MB, RF, RB
Data collection: SvB, DL, AV, WW, RB
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Critical revision of the article: SvB, DL, AV, WW, MB, RF, RB

Final approval of the article: SvB, DL, AV, WW, MB, RF, RB

Statistical analysis: SvB, MB

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Overall responsibility: RB

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Supplementary Table I (online only). Univariable analysis of categoric preoperative patient-related, aneurysm-related, and operation-related characteristics on 5-year survival after endovascular aneurysm repair (EVAR)

Variable	*No.*	*5-year survival, %*	P[a]	*Missing data, % (No.)*
Sex[b]				
Male	386	67	.17	0
Female	47	54		
Pulmonary comorbidity				
Yes	120	63	.36	7 (30/433)
No	283	66		
Cardiac comorbidity[b]				
Yes	246	60	.02	3 (13/433)
No	174	72		
Diabetes				
Yes	60	65	.88	2 (8/433)
No	365	65		
Hypertension				
Yes	157	66	.89	3 (13/433)
No	263	63		
Cerebrovascular comorbidity[b]				
Yes	57	61	.17	1 (4/433)
No	372	66		
Hypercholesterolemia				
Yes	169	64	.93	3 (15/433)
No	249	66		
Previous history of malignancy[b]				
Yes	101	52	<.01	0
No	332	69		
Current smoking				
Yes	155	59	.12	17 (74/433)
No	204	67		
Use of statin				
Yes	203	60	.12	12 (54/433)
No	176	70		
Use of oral anticoagulants[c]				
Yes	262	64	.73	12 (54/433)
No	117	65		
Anemia[b]				
Yes	111	56	.01	2 (9/433)
No	313	69		
ASA score[b]				
1	10	100	<.01	0
2	162	78		
3	243	57		
4	18	46		
Aneurysm characteristics				
Thrombus or calcification in the infrarenal neck				
Yes	202	67	.52	20 (87/433)
No	144	65		
Iliac calcification				
Moderate/severe	228	63	.51	21 (89/433)
None/mild	116	69		
Operating characteristics				
Anesthesia				
General	353	66	.81	8 (36/433)
Locoregional	44	65		
Graft generation				
Early	163	60	.19	8 (34/433)
Late	236	68		
Adjunctive or ancillary procedure[b]				
Yes	86	56	.03	0
No	347	68		

ASA, American Society of Anesthesiologists; *ISCS,* International Society for Cardiovascular Surgery; *SVS,* Society for Vascular Surgery.
[a]Log-rank test.
[b]Included in multivariable Cox proportional hazards model (Table III).
[c]Platelet aggregation inhibitor or vitamin K antagonist.

Supplementary Table II (online only). Univariable analysis of continuous preoperative patient-related, aneurysm-related, and operation-related characteristics on 5-year survival after endovascular aneurysm repair (EVAR)

Patient characteristics	*Mean*	*Hazard ratio*	P[a]	*Missing data, % (No.)*
Age,[b] years	73.9	1.05	<.01	0
BMI, kg/m^2	26.1	0.92	<.01	15 (67/433)
Serum creatinine,[b] μmol/L	93	1.01	<.01	0
Aneurysm characteristics				
Maximum aneurysm diameter,[b] mm	62	1.03	<.01	0
Length infrarenal neck, mm	33	0.99	.05	19 (83/433)
Diameter infrarenal neck, mm	24	1.02	.61	19 (83/433)
Maximum AP/lateral infrarenal neck angulation,°	29	1.00	.87	19 (83/433)
Maximum AP/lateral aneurysm angulation, °	43	1.00	.48	19 (83/433)

AP, Anteroposterior; *BMI,* body mass index.
[a]Univariable Cox proportional hazards model.
[b]Included in multivariable Cox proportional hazards model (Table III).

Supplementary Table III (online only). Multivariable Cox regression model to assess the association between endograft generation (early vs late) and reinterventions, including conversions to open repair (OR)[a]

Variable	*No.*	*Hazard ratio*	*95% CI*	P
Infrarenal neck angulation >45°		1.59	0.86-2.93	.14
Infrarenal neck diameter, mm				
<22	71	0.82	0.35-1.91	.64
22-26	170	1.33	0.69-2.56	.39
>26	85	Reference		
Infrarenal neck length, mm				
<24	88	2.16	0.97-4.81	.06
24-43	160	1.53	0.72-3.26	.27
>43	78	Reference		
Late-generation endograft		0.49	0.29-0.84	.01

CI, Confidence interval.
[a]The model included 326 patients and 55 events, −2 log likelihood (LL), 591.

Supplementary Table IV (online only). Multivariable Cox regression model to assess the association between endograft generation (early vs late) and a combined end point of death and reinterventions, including conversions to open repair (OR)[a]

Variable	*No.*	*Hazard ratio*	*95% CI*	P
Age, years				
<69	86	Reference		
69-79	157	0.99	0.63-1.54	.95
>79	73	1.36	0.80-2.30	.25
Female sex		1.16	0.68-2.00	.53
Previous history of malignancy		1.66	1.14-2.43	<.01
ASA 3 or 4		1.39	0.95-2.03	.09
AAA diameter, mm				
<61	159	Reference		
61-67	76	1.18	0.76-1.83	.46
>67	81	1.49	0.98-2.28	.06
Infrarenal neck angulation >45°		1.10	0.72-1.69	.66
Infrarenal neck diameter, mm				
<22	66	1.07	0.62-1.84	.81
22-26	167	1.34	0.87-2.06	.18
>26	83	Reference		
Infrarenal neck length, mm				
<24	86	2.03	1.22-3.37	<.01
24-43	153	1.40	0.87-2.25	.17
>43	77	Reference		
Year of intervention				
<2004	95	Reference		
2004-2006	105	1.15	0.81-1.85	.58
>2006	126	0.97	0.62-1.54	.91
Late-generation endograft		0.58	0.39-0.86	<.01

AAA, abdominal aortic aneurysm; *ASA,* American Society of Anesthesiologists; *CI,* confidence interval.
[a]The model included 316 patients and 139 events, −2 log likelihood (LL), 1479.